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Research letter

External Heated Humidification During Non-Invasive Ventilation Set Up: Results from a pilot cross-over clinical trial

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External Heated Humidification During Non-Invasive Ventilation Set Up:

Results from a pilot cross-over clinical trial

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Take Home Message: Short-term heated humidification has limited effect on physiological and clinical outcomes during non-invasive ventilation set up

Keywords: non-invasive ventilation, chronic respiratory failure, humidification

INTRODUCTION

Patient comfort is important in ensuring adherence to domiciliary non-invasive ventilation (NIV). Oronasal dryness is often reported with NIV use [1], but the use of heated humidification in clinical practice is not uniform [2]. As there are limited data to currently guide clinical practice, we investigated the effect of external heated humidification on neural respiratory drive (NRD), patient-ventilator asynchrony (PVA), patient-reported outcomes, ventilator performance and adherence in a pilot randomised cross-over trial in patients with chronic respiratory failure during NIV set up.

METHODS

The study was approved by the local research ethics committee (11/H0802/10) and registered on clinicaltrials.gov (NCT01372072). Patients with a new diagnosis of chronic respiratory failure and sleep-disordered breathing were screened for inclusion into the trial. Following the obtaining of written informed consent, subjects were randomised (sealed envelope method). Patients were allocated to receive NIV with heated humidification **(HH+)** or without **(HH-)** heated humidification with an RT040 face mask (Fisher & Paykel, New Zealand). Ventilator settings were set as per local protocol [3]. Patients received **HH+** NIV or **HH-** NIV for 3 weeks, followed by a 2-week wash-out period and then crossed over to the opposite arm of the trial for a further 3 weeks. Temperature setting was adjusted according to patient comfort with no changes in settings during the study nights. NIV adherence was the principal outcome.

NRD was measured using 2nd intercostal space parasternal electromyography (EMG_{para}, $EMG_{para\%max}$) as previously described [4] and PVA was measured as previously reported [5].

Transcutaneous carbon dioxide ($TcCO_2$) and oxygen saturations (SpO_2) were measured (Radiometer Medical, Copenhagen, Denmark). Health related quality of life and daytime somnolence were assessed using severe respiratory insufficiency (SRI) questionnaire and Epworth sleepiness score (ESS), respectively.

A Wilcoxon signed-rank test was used to compare differences between groups and Friedman analysis with Dunn's post hoc analysis for comparisons from baseline (i.e. pre-NIV). Estimates were reported using medians and interquartile range. An intention to treat analysis was performed for NIV adherence. All statistical analyses were performed using Graphpad version 5.0 (Graphpad software Inc, California, USA).

RESULTS

Fifteen patients were recruited, age 59 (50-66) years, BMI 41.2 (28.5-47.1) $kg.m^{-2}$, 6 male patients, (5 COPD, 8 obesity hypoventilation syndrome and 2 chest wall disease). 2 subjects were unable to tolerate **HH+.** Inspiratory positive airways pressure **(**IPAP) was 24 ± 5 cmH_2O with expiratory positive airways pressure (EPAP) of 8 ± 4 cmH_2O and inspiratory time (Ti) of 1.2 ± 0.1s and a back-up rate of 13 ± 3 bpm (93% patients pressure support (PS) mode, 7% patients pressure-controlled (PC) mode).

NIV adherence, patient reported outcome scores, gas exchange, NRD and PVA

There was no between-group difference in 3-week NIV adherence (**HH+** 283 (156-403) mins/night *vs.* **HH-** 307 (69-335) mins/night, p=0.74). The Epworth sleepiness score improved in both **HH-** and **HH+** but there was no between group difference (**ΔHH-** 4.9 ± 4.8 vs. **ΔHH+** 4.5 ± 4.6; p = 0.41). There was a small increase in SRI at 3 weeks in **HH+** group, but these differences were not observed in the **HH-** group (*Table 1*).

There was a reduction in nocturnal $TcCO_2$ from baseline in both **HH+** and **HH-** groups ($TcCO_2$ Δ**HH+** -1.7 (-2.5 to -1.0) kPa, p=0.0005; Δ**HH-** -1.5(-2.5 to-0.6) kPa, p=0.0034), but there was no between group difference observed (p=0.39).

There was a reduction in mean nocturnal $EMG_{para\%max}$ observed in both groups compared to the baseline self-ventilation night (baseline 16% (12-26) *vs.* **HH+** 6% (5-8) p=0.002; baseline 13% (11-20) *vs*. **HH-** 6% (4-9) p=0.0005). Importantly, there was a difference observed in $\Delta EMG_{para\%max}$ between the **HH+** and **HH-** with a greater reduction in the **HH+** group (**ΔHH+** -10.7 (-17.7 to -5.4)% vs. **ΔHH-** -2.2 (-3.8 to 0.2)%; p=0.001).

Comparison of the set IPAP (24 ± 5cmH_2O) and mask pressure showed delivered IPAP showed much lower IPAP in the **HH+** group (**ΔHH+** -8.4 cmH_2O (-10.3 to -2.9, p=ns); **ΔHH-** -4.4 cmH_2O (-8.2 to -1.0, p=ns) with significant difference between **ΔHH+** and **ΔHH-**; p=0.03). 22,831 breaths were analysed for PVA (*Table 1*) with 100% of patients observed to have an asynchrony index >10 events per hour in the **HH+** group compared to 79% in the **HH-** group, although these was no significant difference (p=0.4). There was no between group difference in type or proportion of PVA, although total PVA was greatest in the **HH+** group (p=0.009; *Table 1*).

DISCUSSION

These data have demonstrated short-term NIV adherence of patients with chronic respiratory failure is not enhanced by heated humidification during NIV set up. Furthermore, NIV with and without heated humidification, showed similar improvements in neural respiratory drive and overnight gas exchange, health-related quality of life and daytime somnolence. Of clinical relevance, 13% of patients were unable to tolerate heated

humidification with a reduction in ventilator driving pressure observed, compared to the set pressure, with heated humidification (mean reduction of 4cmH_2O). This is a consequence of the addition of a heated humidification chamber, increasing the ventilator circuit volume and dead space. The effect of an integrated humidifier in the newer devices is unknown. The authors acknowledge that the pressure drop may have been, in part, as a result of mask leak, but that the leak would be expected with and without heated humidification.

It was interesting to observe that despite a higher frequency of patient-ventilator asynchrony in the heated humidification group, there was a reduction in NRD overnight compared to the group without humidification. Although there was a statistical difference with and without humidification at 3 weeks (8.5% mean nocturnal $EMG_{para\%max}$ difference) this was only a small absolute difference between the groups (Δ**HH+** -5.3 vs. **HH-** Δ-4.6µV). Furthermore, the reduction in NRD from baseline in the heated humidification group was greater compared to the group without humidification (10% vs. 7%) and, importantly, the reduction from baseline was not sustained in the group without humidification despite the less frequent asynchrony events, which suggests that the heated humidification effect on NRD is both immediate and sustained, at least, in the short-term. Although not objectively measured in this study, patient comfort measures should be measured in future. Based on these current data, future trial design for assessment of the effect of heated humidification would be to focus on those patients with chronic respiratory failure that have low short-term NIV adherence as a consequence of oronasal dryness despite tolerating in hospital NIV set up. This provides a more clinically relevant target population for the use of heated humidification.

The authors acknowledge that these pilot data report a limited number of patients with a mixture of causes of chronic respiratory failure. However, there is a paucity of data detailing the short-term physiological effect of heated humidification on neural respiratory drive, ventilator performance and patient-ventilator interaction as well as the clinical effect on overnight gas exchange and ventilator adherence. The current data provides the platform to design a randomised controlled trial to investigate the clinical and cost effectiveness of heated humidification during NIV set up similar to design of previous trials [6].

Conclusion

These clinical data, from a pilot randomised cross-over trial, have shown that external heated humidification during NIV set up has limited effect on short-term clinical outcomes, such as overnight gas exchange, health-related quality of life and NIV adherence. In addition, the clinician needs to acknowledge that external humidification negatively impacts ventilator pressure delivery. Future longterm trials of heated humidification should target those patients reporting low short-term NIV adherence as a consequence of oronasal dryness.

Competing interests: none

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Table 1: Patient reported outcome scores and patient ventilator asynchrony

	Baseline (n=12)	Heated Humidification (HH+) (n=12)	No humidification (HH-) (n=12)
ESS (/24)	12 (9-17)	6 (5-11)*	7 (4-12)*
NIV side effect score (/44)	NA	6 (5-9)	6 (5-9)
SRI-RC	59 (33-77)	72 (63-89)	71 (42-85)
SRI-PF	50 (44-79)	58 (40-83)	58 (42-79)
SRI-AS*	50 (23-57)	61 (39-70)*	54 (45-66)
SRI-SR	75 (52-85)	71 (52-88)	67 (54-88)
SRI-AX*	45 (23-68)	60 (48-90)*	60 (43-70)
SRI-PWB	58 (47-64)	61 (47-71)	61 (42-79)
SRI-SF	69 (45-80)	69 (50-81)	63 (55-86)
SRI-SS*	61 (40-68)	64 (50-76)*	60 (50-80)

Patient Ventilator Asynchrony (%)

	Baseline	n=12	n=14
Ineffective efforts	-	18.2 (1.1-23.8)	3.2 (0-22.5)
Auto-triggering	-	37.0 (6.7-54.2)	21.7 (6.2-37.0)
Double triggering	-	0 (0-0.3)	0.1 (0-0.2)
Total triggering PVA	-	39.3 (6.7-55.0)	21.7 (6.2-37.5)
Premature cycling	-	1.0 (0.4-1.8)	0.5 (0.1-2.5)
Delayed cycling	-	0.9 (0-2.7)	0.3 (0-3.6)
Total cycling PVA	-	3.8 (2.2-8.2)	2.0 (0.9-7.1)
Total PVA	-	57.1 (32.3-73.7)	34.3 (11.6-74.6)*

**p<0.05 from baseline. Abbreviations RC=respiratory components, PF=physical functioning, AS=attendant symptoms and sleep, SR=social relationships, AX=anxiety, PWB=psychological well-being, SF=social functioning, SS=sum score*